REMARKS/ARGUMENTS

Claims 1, 22, 23, and 24 are pending. Claims 2-22 have been cancelled without prejudice.

A Request for Continued Examination has been made for *inter alia* the filing an Information Disclosure Statement to provide the following references cited in the pending European Search Report to the Examiner for consideration.

WO 02/099068 A

WO 2005/030985 A

MEMON R A et al. DIABETS, NEW YORK, NY, US, Vol.48, No. 1, January 1999 pages 121-127 "Regulation of Putative Fatty Acid Transporters and Acyl-Coa Synthetase in Liver and Adipose Tissue in ob/ob Mice"

INAGAKI KATSUYA et al. BIOSCIENCE BIOTECHNOLOGY AND BIOCHEMISTRY vol. 66, No. 3, March 2002 pages 613-621 "Identification and expression of a rat fatty acid elongase involved in the biosynthesis of C18 fatty acids"

I. Claim Rejection under U.S.C. § 103(a)

Claims 1 and 22-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Moon et al. (J.Biol. Chem. 276: 45,358-45,366 (2001) in view of Matsuzuka et al. (J. Lipid Res. 43: 911-920 (2002).

The applicants respectfully disagree. The prior art does not suggest the applicants discovery, "a fixed correlation between weight change and LCE expression," that is, the prior art does not disclose any data which directly indicate a connection between LCE expression and obesity.

Matsuzaka discloses adipose and overexpression of LCE are simultaneously observed in the liver of ob/ob mice, but does not disclose the causation and consequence of those phenomenon. Matsuzaka describes that FACE could be related to human obesity and also that there could be a relationship between obesity and LCE. The rejection includes several passages from Matsuzaka in support; however, these passages are not believed to support the instant rejection. While Matsuzuka showed that FACE mRNA levels were elevated in ob/ob mice compared to wild-type mice, the levels of FACE mRNA in WAT appeared to be same in both ob/ob mice and wild-type mice (page 18, first full paragraph). The conclusions drawn by

Matsuzuka appear to be merely invitations to experiment. In other words, invitations to figure out whether FACE expression is indeed directly correlated with obesity such that inhibition of FACE expression would consequentially produce a reduction in obesity to an extent that would make inhibition of FACE a viable treatment for obesity. For example, on page 919, in the discussion, Matsuzaka states

> Theoretically, the role of FACE in lipogenesis seems crucial because no other known enzymes have been reported to show the same activity as observed in this enzyme. However, the importance of this gene in lipogenesis as an energy storage system or in more basal cellular functions awaits analysis of effects of the FACE gene disruption, such as characterization of gene knockout mice.

On page 919, Matsuzaka concludes the discussion by stating

> It was reported that elongase activity estimated by C18:0-C16:0 ratio in the muscle is significantly related to adiposity in humans (42), suggesting that FACE could be related to human obesity. Further studies might unveil clinical relevance of FACE to human diseases or pathophysiological states.

The above statements appear to be invitations to experiment and not recitations of an actual correlation between LCE activity and obesity. Matsuzaka does not state that the elevation of LCE activity fosters obesity. In Matsuzaka there is no suggestion or teaching that suppressing LCE activity will lead to an anti-obesity effect or that elevating LCE activity will lead to obesity. The rejection appears to presume that there is relationship between LCE and obesity based on the coincidence of the changes between LCE and obesity over time; however, the presumption is theoretically incorrect and these two parameters should be differently evaluated. The coincidence of the changes between LCE and obesity over time is a phenomenon that may be because (1) there is no relationship between LCE and obesity but both phenomenon occur simultaneously by any reason other than the relationship; (2) obesity leads to the elevation of LCE activity; or (3) overexpression of LCE leads to obesity. Matsuzaka neither prove nor suggest the direct relationship between LCE and obesity. A direct relationship between LCE and obesity may be proved by showing the overexpression leads to the increase of body weight, or the suppression of LCE expression leads to the decrease of body weight or the suppression of body weight increase. Neither of these are shown or suggested by Matsuzaka.

The present invention proves for the first time that there is a direct relationship (that is, causation and consequence) of LCE activity and body weight, namely that overexpression of LCE leads to an increase of body weight and that suppression of LCE activity

has an anti-obesity effect. This based upon the applicants' experiments that show that a decrease in LCE activity ameliorates the parameters of obesity, for example , see Fig. 11A and Fig. 18.

It is generally understood that when the LCE activity, which changes C16 fatty acids into C18 fatty acids, is inhibited, the amount of C18 fatty acids (reaction product) is decreased but the amount of C16 fatty acids (substrate) is increased. Thus, it is arguably expected that the composition of each fatty acid, not the total amount of fatty acid, is changed, but the change of the total amount of fatty acids is not expected. The present invention proves for the first time the relationship of LCE activity and the changes in total amount of fatty acids.

The rejection included Moon for the disclosure that "SREBP-1a(TgSREBP-1a) transgenic mice manifested large fatty livers" to arguably show the relationship between LCE activity and obesity. However, it is well known that fatty liver is different from obesity, such as shown in the MERCK MANUAL [16th edition], Pathogenesis in Chapter 69, pages 851-852, which describes fatty liver as being caused by many reasons, such as obesity, chemical material (alcohol, steroid etc.), malnutrition, pregnancy, etc. and Pathophysiology in Chapter 80, page 919-920, describing fatty liver caused by malnutrition, and in Angulo, New England J. Med. 2002 Apr 18; 346(16):1221-31, which strates "Regardless of body-mass index, the presence of type 2 diabetes mellitus significantly increases the risk and severity of nonalcoholic fatty liver disease."

It is generally well known that when body weight is decreased due to malnutrition, fatty liver is observed. Thus, Moon neither discloses the relationship between the overexpression of LCE and weight gain, nor the expectation that inhibitor of LCE activity leads anti-obesity effects.

Therefore, because the prior art does not teach a correlation between obesity and expression of LCE, it would have been unlikely that a person of ordinary skill in the art in view of the prior art would have had a reasonable expectation that finding an inhibitor of LCE activity as taught by the applicants would provide a candidate that could be used for treating obesity or inhibiting weight gain. In light of the above, reconsideration of the rejection is requested.

Favorable action is earnestly solicited.

CONDITIONAL PETITION

Applicant hereby makes a Conditional Petition for any relief available to correct any defect in connection with this filing, or any defect remaining in this application after this filing. The Commissioner is authorized to charge deposit account 13-2755 for the petition fee and any other fee(s) required to effect this Conditional Petition.

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Respectfully submitted,

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